

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-13, 18-21 and 28 are pending in the application, with claims 1, 2, 6 and 7 being the independent claims. Claims 14-17 and 22-27 are sought to be canceled without prejudice to or disclaimer of the subject matter therein. Claims 1, 2 and 4-7 are sought to be amended. Support for the claim amendments can be found throughout the specification and in the claims as originally presented. For example, support for the amendment to claims 1, 2, 6 and 7, specifying that the medium is devoid of animal proteins, can be found at page 6, lines 1-2. No new matter is added by way of these amendments. It is respectfully requested that the amendments be entered and considered.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

I. IDS Document AT2

On the Examiner-initialed FORM PTO-1449 that was attached to the Office Action, document AT2 (Healy and Macmorine, 1972) was crossed out with the notation "no copy provided" handwritten in the margin. Applicants note that a copy of Healy and Macmorine, 1972 was submitted as document "AS10" with the First Supplemental Information Disclosure Statement filed on April 30, 2003, in the parent application, U.S. 09/693,949. A copy of the Examiner-initialed FORM PTO-1449, acknowledging consideration of this

document in the parent application is attached hereto as Exhibit 1. Thus, in accordance with 37 C.F.R. § 1.98(d), a copy of this document was not submitted with the IDS that was filed in the present application on August 31, 2004. Nonetheless, for the Examiner's convenience, a copy of the Healy and Macmorine, 1972 reference is attached hereto as Exhibit 2. Applicants respectfully request that the Examiner consider this reference and indicate in the next official communication that this reference has been considered.

II. Priority

A. Priority Claim

The Examiner stated that Applicants need to correct the first page of the specification to correctly indicate how U.S. Patent Appl. No. 09/302,953 is related to its parent cases. The Examiner also stated that U.S. Patent Appl. No. 09/070,807 does not exist in the USPTO records. *See* Office Action, page 2.

Applicants note that U.S. Patent Appl. No. 09/070,807 was converted to U.S. Provisional Application No. 60/183,031 on March 21, 2000. A copy of the Decision on Petition to convert U.S. Patent Application No. 09/070,807 to a provisional application is attached hereto as Exhibit 3. U.S. Patent Appl. No. 09/302,953 was filed on April 30, 1999, which is less than one year from the filing date of the '807 application (May 1, 1998), but *before* the Decision on Petition was granted.

Thus, although the first sentence of the specification for U.S. Patent Appl. No. 09/302,953 indicates that the '953 application claims priority to, *inter alia*, U.S. Patent Appl. No. 09/070,807, the '953 application should be regarded as claiming the benefit of

Provisional Appl. No. 60/183,031. The priority claim for the present application has been corrected accordingly by amending the first sentence of the specification and by submitting a Supplemental Application Data Sheet herewith.

B. Support for Stigmasterol

The Examiner stated that the disclosure of U.S. Patent 6,103,529 does not support using stigmasterol in the culture media, and therefore, according to the Examiner, "claims to this ingredient are only given a priority date to the filing date of 09/302,953 which is April 30, 1999." *See* Office Action, pages 2-3. Applicants note that Provisional Application No. 60/183,031 (which was converted from U.S. Application No. 09/070,807, filed May 1, 1998) fully supports the inclusion of stigmasterol in the culture media of the invention. *See, e.g.*, page 18, line 29, of the 60/183,031 specification. Thus, claims directed to subject matter that includes stigmasterol are entitled to the benefit of the filing date of the 60/183,031 application; *i.e.*, May 1, 1998.

III. Double Patenting

Claims 1-9, 12, 13, 18-21 and 26-28 were rejected under the judicially-created doctrine of obviousness-type double patenting over the claims of U.S. Patent No. 6,103,529. *See* Office Action, page 3. Applicants respectfully request that this rejection be held in abeyance until the remaining issues in this application are resolved, at which time Applicants will consider submitting a terminal disclaimer over the '529 patent.

IV. Claim Rejections Under 35 U.S.C. § 102

A. WO 98/24883

Claims 2, 7, 10, 11 and 28 were rejected under 35 U.S.C. § 102(a) as being anticipated by WO 98/24883 in view of the English language abstract of JP 2000175643. *See* Office Action, page 4. Applicants respectfully traverse this rejection.

As noted above, the present application -- including subject matter that includes stigmasterol -- is entitled to the benefit of the filing date of U.S. Provisional Patent Application No. 60/183,031, filed May 1, 1998. The publication date of WO 98/24883 is June 11, 1998. Thus, WO 98/24883 is not prior art to the present application. Applicants therefore respectfully request that this rejection be withdrawn.

B. Iscove in light of JP Pat. No. 34002673

Claims 2, 7, 10, 11, 13, 20, 21, 26 and 28 were rejected under 35 U.S.C. § 102(b) as being anticipated by Iscove *et al.*, *J. Exp. Med.* 147:923-933 (1978) ("Iscove"), in light of CAPLUS abstract of Japanese Pat. No. 34002673 (1959). *See* Office Action, page 5. Applicants respectfully traverse this rejection.

The Examiner stated that "Iscove teaches a culture medium for B lymphocytes that contains soybean lipids," and that "JP '673 teaches that soybean [inherently] contains the sterol stigmasterol. Thus, the culture medium of Iscove would inherently contain stigmasterol." *See* Office Action, page 5.

Independent claims 2 and 7, as currently presented, specify that the culture medium is *devoid of animal proteins*. By contrast, the culture media used in the experiments of

Iscove contained, in addition to soybean lipid, albumin and transferrin. *See, e.g.*, Iscove, page 925, second full paragraph under *Results*, and page 927, third full paragraph from the top. Albumin and transferrin are animal proteins. *See, e.g.*, Iscove, page 924, under *Materials and Methods* (indicating that the transferrin was human transferrin and that the albumin was bovine serum albumin). Iscove does not teach a cell culture medium devoid of animal proteins comprising plant derived lipids. Accordingly, Iscove does not anticipate claims 2 or 7 or any of the claims that depend therefrom. Applicants respectfully request that this rejection be reconsidered and withdrawn.

C. Keay

Claims 1, 6, 12, 18, 19, 26 and 27 were rejected under 35 U.S.C. § 102(b) as being anticipated by Keay, *Biotech. Bioeng.* 17:745-764 (1975) ("Keay"). *See* Office Action, page 5. According to the Examiner, "Keay teaches that soy peptone can be used to culture animal cells." *See id.* Applicants respectfully traverse this rejection.

Independent claims 1 and 6, as currently presented, specify that the non-animal or plant-derived peptide included in the claimed culture media is derived from any one of bacteria, fungi, yeast, rice, potato, corn or aloe vera. Keay does not teach a cell culture medium comprising a non-animal or plant-derived peptide derived from bacteria, fungi, yeast, rice, potato, corn or aloe vera. Thus, Keay does not anticipate claims 1 or 6 or any of the claims that depend therefrom. Applicants respectfully request that this rejection be reconsidered and withdrawn.

D. U.S. Pat. No. 5,741,705

Claims 1, 6, 12, 18, 19, 26 and 27 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Pat. No. 5,741,705. *See* Office Action, page 6. According to the Examiner, "US '705 teaches an animal cell culture medium that contains rice proteins." *See id.* Applicants respectfully traverse this rejection.

Independent claims 1 and 6, as currently presented, specify that the culture medium is *devoid of animal proteins*. Claims 1 and 6 also specify that the medium is capable of supporting the cultivation of an animal cell *in vitro*.

The '705 patent relates to the use of hydrolyzed protein material in eukaryotic culture media. *See* the '705 patent, column 2, lines 56-61. Although the '705 patent, at column 3, lines 43-46, mentions that the "protein raw material" to be hydrolyzed may be "rice proteins," there is no indication in the '705 patent that a culture medium *devoid of animal proteins* containing hydrolyzed rice protein (or any non-animal or plant-derived peptides) would be capable of supporting the cultivation of an animal cell *in vitro*. In fact, the medium used in the examples of the '705 patent was RPMI-1640 medium containing a supplement that included 8% fetal bovine serum. *See* the '705 patent, column 6, line 41, through column 7, line 3, and column 8, lines 35-55. Thus, it appears that serum (which contain animal proteins) was required in the media of the '705 patent.

Since the '705 patent does not teach a cell culture medium devoid of animal proteins that is capable of supporting the cultivation of an animal cell *in vitro*, the '705 patent does not anticipate claims 1 or 6 or any of the claims that depend therefrom. Applicants respectfully request that this rejection be reconsidered and withdrawn.

V. Claim Rejections Under 35 U.S.C. § 103

A. U.S. Pat. No. 5,741,705 and WO 98/24883

Claims 1 and 3 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pat. No. 5,741,705 and WO 98/24883. *See* Office Action, page 6. Applicants respectfully traverse this rejection.

A *prima facie* case of obviousness cannot be established unless all of the claim elements are taught or suggested by the cited references. *See In re Royka*, 490 F.2d 981, 984-85 (CCPA 1974); *see also In re Glaug*, 283 F.3d 1335, 1341-42 (Fed. Cir. 2002); *In re Rijckaert*, 9 F.3d 1531, 1533 (Fed. Cir. 1993). In addition, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. *See In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998).

As noted above, WO 98/24883 is not prior art to the present application. In addition, the '705 patent does not teach or suggest a cell culture medium devoid of animal proteins that is capable of supporting the cultivation of an animal cell *in vitro*. Moreover, the '705 patent is silent with respect to the use of non-animal or plant-derived lipids or fatty acids as recited in claim 3. Thus, not all elements of the present claims are taught or suggested by the '705 patent. Additionally, no evidence has been presented to indicate that a person of ordinary skill in the art would have been motivated in any way to modify the '705 patent. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

B. Iscove in view of U.S. Pat. No. 5,266,479

Claims 1 and 4 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Iscove in view of U.S. Pat. No. 5,266,479. *See* Office Action, page 7. Applicants respectfully traverse this rejection.

Neither Iscove nor the '479 patent teaches or suggests a cell culture medium devoid of animal proteins comprising at least one non-animal or plant-derived peptide. As noted above, the culture media of Iscove contained albumin and transferrin. Similarly, the medium of the '479 patent includes animal-derived proteins such as bovine serum albumin, bovine insulin and human transferrin. *See* the '479 patent, table bridging columns 9-10. Thus, not all of the elements of claims 1 or 4 are taught or suggested by the cited references. In addition, a person of ordinary skill in the art would not have been motivated to modify or combine the cited references. Consequently, a *prima facie* case of obviousness has not been established. Applicants respectfully request that this rejection be reconsidered and withdrawn.

C. U.S. Pat. No. 5,741,705 in view of U.S. Pat. No. 5,266,479

Claims 1 and 4 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pat. No. 5,741,705 in view of U.S. Pat. No. 5,266,479. *See* Office Action, page 8. Applicants respectfully traverse this rejection.

Neither the '705 patent nor the '479 patent teach or suggest a cell culture medium devoid of animal proteins that is capable of supporting the cultivation of an animal cell *in vitro*. Thus, not all of the elements of claims 1 or 4 are taught or suggested by the cited references. In addition, a person of ordinary skill in the art would not have been motivated

to modify or combine the cited references. Consequently, a *prima facie* case of obviousness has not been established. Applicants respectfully request that this rejection be reconsidered and withdrawn.

D. Keay in view of U.S. Pat. No. 5,266,479

Claims 2 and 5 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Keay in view of U.S. Pat. No. 5,266,479. *See* Office Action, page 8. Applicants respectfully traverse this rejection.

Neither Keay nor the '479 patent teaches or suggests a cell culture medium comprising at least one non-animal derived or plant-derived lipid or at least one non-animal or plant-derived fatty acid. Thus, not all of the elements of claims 2 or 5 are taught or suggested by the cited references. In addition, a person of ordinary skill in the art would not have been motivated to modify or combine the cited references. Consequently, a *prima facie* case of obviousness has not been established. Applicants respectfully request that this rejection be reconsidered and withdrawn.

E. WO 98/24883 in view of U.S. Pat. No. 5,266,479

Claims 2 and 5 were rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 98/24883 in view of U.S. Pat. No. 5,266,479. *See* Office Action, page 8. Applicants respectfully traverse this rejection.

As noted above, WO 98/24883 is not prior art to the present application. In addition, the '479 patent does not teach or suggest a cell culture medium comprising at least one non-animal derived or plant-derived lipid or at least one non-animal or plant-derived fatty acid.

The '479 patent does not teach or suggest a cell culture medium devoid of animal proteins. Thus, not all of the elements of claims 2 or 5 are taught or suggested by the cited references. In addition, a person of ordinary skill in the art would not have been motivated to modify or combine the cited references. Consequently, a *prima facie* case of obviousness has not been established. Applicants respectfully request that this rejection be reconsidered and withdrawn.

F. Keay in view of U.S. Pat. No. 4,533,637

Claims 2, 7 and 9 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Keay in view of U.S. Pat. No. 4,533,637. *See* Office Action, page 9. Applicants respectfully traverse this rejection.

Neither Keay nor the '637 patent teaches or suggests a cell culture medium comprising at least one non-animal derived or plant-derived lipid or at least one non-animal or plant-derived fatty acid. The '637 patent mentions the ingredient "linoleic acid" generically. *See, e.g.*, the '637 patent, column 5, lines 42-54. However, there is no suggestion in the '637 patent to use non-animal or plant-derived fatty acids. Moreover, the medium used in the examples of the '637 patent contained human transferrin. *See, e.g.*, the '637 patent, column 7, line 40. The medium of the '637 patent is therefore *not* devoid of animal proteins. Thus, not all of the elements of claims 2, 7 or 9 are taught or suggested by the cited references. In addition, a person of ordinary skill in the art would not have been motivated to modify or combine the cited references. Consequently, a *prima facie* case of obviousness has not been established. Applicants respectfully request that this rejection be reconsidered and withdrawn.

G. WO 98/24883 in view of U.S. Pat. No. 5,266,479

At page 9 of the Office Action, item 17, it is stated that "[c]laims 2, 7, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keay in view of US Pat. No. 4,533,637." In the paragraph that immediately follows, however, the Examiner refers to "WO '883" and "US '479." Neither Keay nor U.S. Pat. No. 4,533,637 are mentioned in the paragraph under item 17 in the Office Action. It therefore appears that the reference to Keay and U.S. Pat. No. 4,533,637 in item 17 of the Office Action was in error, and that the intended rejection was based on WO 98/24883 and U.S. Pat. No. 5,266,479. Applicants request clarification. Assuming that the intended rejection was based on WO 98/24883 and U.S. Pat. No. 5,266,479, Applicants respectfully traverse this rejection.

As noted above, WO 98/24883 is not prior art to the present application. In addition, the '479 patent does not teach or suggest a cell culture medium comprising at least one non-animal derived or plant-derived lipid or at least one non-animal or plant-derived fatty acid. The '479 patent does not teach or suggest a cell culture medium devoid of animal proteins. Thus, not all of the elements of claims 2, 7 or 9 are taught or suggested by the cited references. In addition, a person of ordinary skill in the art would not have been motivated to modify or combine the cited references. Consequently, a *prima facie* case of obviousness has not been established. Applicants respectfully request that this rejection be reconsidered and withdrawn.

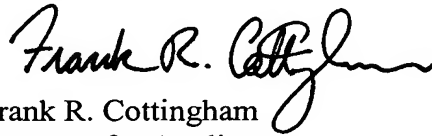
Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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Date: OCT. 12, 2005

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FORM PTO-1449

FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
0942.4120005/RWE/FRCAPPLICATION NO.
09/693,949APPLICANT
PRICE *et al.*FILING DATE
October 23, 2000GROUP
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U.S. PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
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FOREIGN PATENT DOCUMENTS

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| | AL | | | | | | Yes No |
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| | AN | | | | | | Yes No |
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

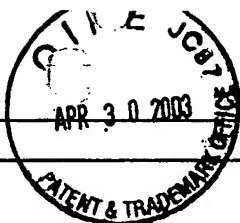
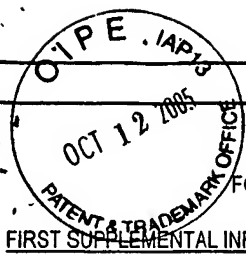
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| | AR | | |
| SC | AS | 10 | Healy, G.M. and Macmorine, H.G., "Replacement of Serum by a Soybean Protein Fraction in a Basal Tissue Culture Medium," <i>Progr. Immunobiol. Standard</i> 5:202-208, Karger (1972). |
| SC | AT | 10 | Partial International Search Report for European Patent Application No. 97910043.5, mailed September 10, 2002. |

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FORM PTO-1449

FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

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FOREIGN PATENT DOCUMENTS

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| SL | AL3 | WO 97/33978 | 09/18/1997 | WIPO | | | Yes No |
| SL | AM3 | WO 98/08934 | 03/05/1998 | WIPO | | | Yes No |
| SL | AN3 | WO 98/30679 | 07/16/1998 | WIPO | | | Yes No |
| | AO | | | | | | Yes No |
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EXAMINER

Howard Lee

DATE CONSIDERED

8-20-03

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered.
Include copy of this form with next communication to Applicant.

Replacement of Serum by a Soybean Protein Fraction in a Basal Tissue Culture Medium

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From the advent of tissue culture in 1907 to the present, blood plasma or blood serum have been an intrinsic part of the media used for the cultivation of animal cells. In the United States every week between 4 and 5 thousand liters of sera are used for tissue culture and virus procedures. Most of these sera are bovine, especially of fetal origin and are produced by commercial suppliers through the co-operation of the abattoirs. The improved growth potential of fetal or newborn sera for cell culture has long been recognized [7]. The efficacy of fetal serum over that of adult has been variously attributed to the following factors: the low lipid content, the absence or a deficiency of γ -globulins, a favourable balance of co-existing growth-promoting and growth-inhibiting proteins, and, of course, the increased likelihood of obtaining blood free from microbial or viral contaminations. In the case of fetal calf serum (FCS), these factors assume even greater significance because the fetal protein is not affected by exchange of proteins between the fetal and maternal circulations [11]. This 'barrier' leads to the accumulation of the fetal bovine protein, fetuin, which has been implicated in the growth-promoting properties of FCS [6]. At one time or another, all these factors have been refuted or open to serious question. KNIAZEFF *et al.* [9] recently reported on the ubiquity of γ -globulins and the frequent occurrence of viruses in FCS.

Until recently little analytical information existed on possible variations in the constituents of FCS that might correlate with its growth-promoting or toxic factors [3, 12]. In April, 1971, the National Cancer Institute, Division of Biologics Standards and the Tissue Culture Association jointly sponsored a workshop dealing with the use of blood serum for tissue culture. At these meetings data were presented on the extent of microbial and viral contamination in various lots of commercial bovine sera [1]. The overall incidence of all such contaminations found in different commercial sources was an alarming 16%. The nature and frequencies of the contaminations are summarized in table I. At the serum workshop certain physico-chemical measurements on different pooled lots of FCS were also reported [2]. The variability of these parameters was greatly in excess of expected values for large pools of individual FCS. These values, together with their ranges, based upon those reported, and on determinations in our own laboratory, are summarized in table II. In contrast, at the special serum

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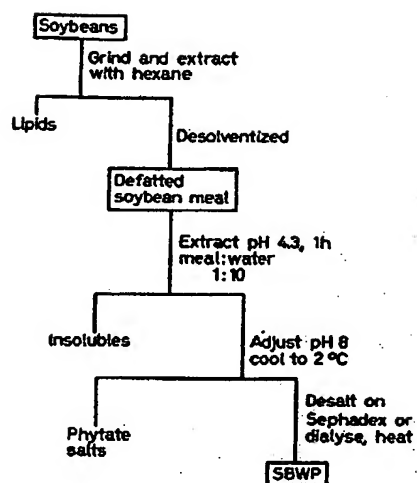


Fig. 1. Procedure followed to prepare SBWP used to supplement the chemically-defined media, CMRL-1969, and BME.

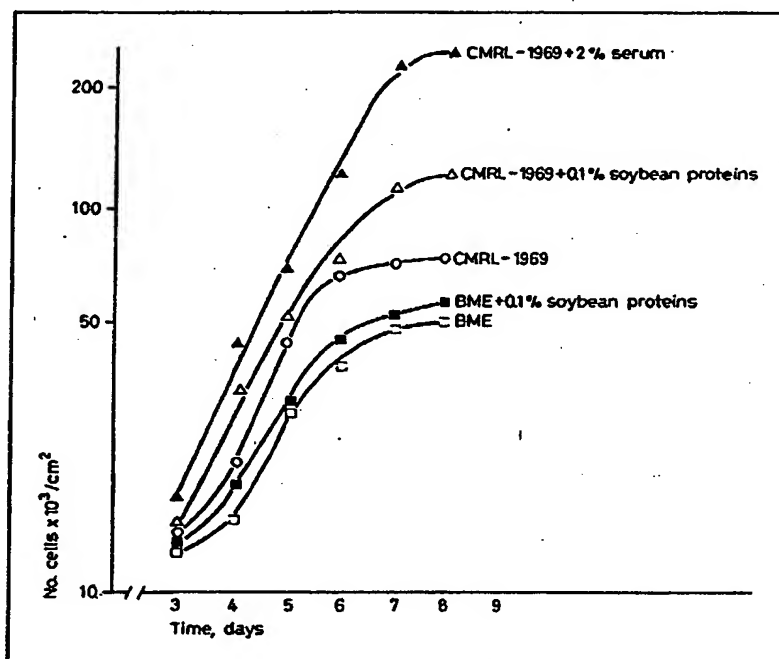


Fig. 2. Growth of PMKC in CMRL-1969 + 2% bovine serum, CMRL-1969 + 0.1% SBWP, CMRL-1969, BME + 0.1% soybean proteins and BME.

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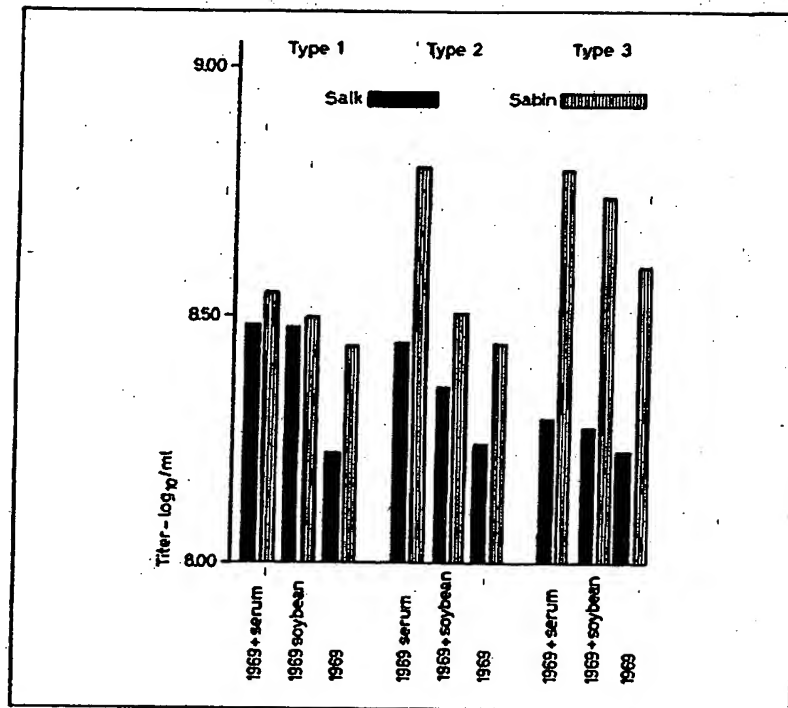


Fig. 4. The live virus titers (geometric mean of 2 independent experiments) for types 1, 2 and 3 of both virulent (Salk) and attenuated (Sabin) polioviruses propagated in separate replicate PMKC cultures in 3 different test media.

neutralized with CMRL-1969 + 5% bovine serum and the cell suspension was washed repeatedly by centrifugation and resuspension in the basal medium. Replicate cultures were prepared in 250-ml flasks, (Falcon Plastics, Division of B-D Laboratories Inc., Los Angeles), containing 40 ml of test medium. To each flask were added: 2 ml of the 5-percent, washed cell suspension in the basal medium and the flasks were incubated at 37 °C. Commencing on the 3rd day, the cell population of each test medium was obtained each day by counting portions of the entire population of trypsin dispersed cells from individual replicate cultures in a hemocytometer. On the 7th day replicate cultures of the series were infected individually with all three types of attenuated (Sabin) poliovirus respectively and incubated at 35 °C. On the 8th day other replicate cultures of the series were infected individually with all three types of virulent (Salk) poliovirus respectively and incubated at 37 °C. Incubation was continued with both sets until the cells were rounded (approximately 48 h) when the entire contents were removed and frozen to await titration of live virus and complement fixing virus. In this way the relative growth and the extent of virus multiplication in CMRL-1969, CMRL-1969 + 0.1% SBWP, and CMRL-1969 + 2% bovine serum were compared. In some experiments basal medium Eagle (BME) and BME + 0.1% SBWP were also included for comparison. BME was purchased in the powdered form from Grand Island Biological Co., New York.

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In re Application of:
Paul Price, et al.
Application No.: 09/070,807
Filed: May 1, 1998
Attorney Docket: 0942.4120002

DECISION ON PETITION

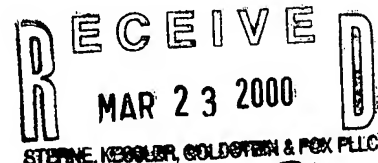
This is a decision on your petition received in the Patent and Trademark Office on June 19, 1998, and treated as a petition under 37 CFR 1.53(b)(2)(ii) to convert the above identified application to a Provisional application under 35 U.S.C. 111 (b) and 37 CFR 1.53(b)(2).

The petition is granted.

The application will be processed in the Office of Initial Patent Examination (OIPE) as a Provisional application under 35 U.S.C. 111(b) and 37 CFR 1.53(b)(2), including the assignment of a new Provisional application number.

The Provisional application serial number is 60/183,031 the filing receipt for the Provisional application number will be communicated to applicant by OIPE in due course.

Betty L. Robinson, Program Assistant
Office of Initial Patent Examination
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3/23 RUT
3/24 BJD